Cocaine

2ß-Carbomethoxy-3ß-(3,4-dichlorophenyl)-bicyclo[3.2.1]octane

2β-Carbomethoxy-3β-(3,4-dichlorophenyl)-8-oxabicyclo[3.2.1]octane

2β-Carbomethoxy-3β-(3,4-dichlorophenyl)-7β-hydroxy-8-methyl-8-azabicyclo(3.2.1)octane

CH3N

2B-Carbomethoxy-3B-(3,4-dichlorophenyl)-6P-hydroxy-8-methyl-8-azablcyclo[3.2.1]octane

Figure 1. Structures of Lead Bicyclo[3.2.1]octanes

Figure 2. Absolute Configurations of (1R)-8a, (1R)-18a, (1S)-18a

Figure 3

Scheme 1. Synthetic Route to 2,3-Unsaturated Tropanes^a

Ar: a = 3,4-Cl₂ phenyl b = 2-Naphthyl c = 4-F-phenyl d = Phenyl

^a Reagents: (i) H₂NCH₃; (ii) CH₂(OCH₃)₂, pTSA; (iii) NaN(TMS)₂, PhNTf₂; (iv) Pd₂(dba)₃, ArB(OH)₂; (v) TMSBr.

3 a. 6-MOM b. 7-MOM

Scheme 2. Synthetic Route to Bridge Oxygenated Tropanes^a

^a Reagents: (i) SmI₂; (ii) TMSBr, CH₂Cl₂; (iii) N-CH₃-morpholine-N-oxide, tetra-n-propylammoniumperruthenate.

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CO₂CH₃

SH3N

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Scheme 3. Synthetic Route to Bridge Oxygenated 2-Keto Tropanes³

12a

CH₃N CON(CH₃)OCH₃ MOMO

CH₃N CON(CH₃)OCH₃
MOMO

CH₃N COC₂H₅

MOMO

CH₃N COC₂H₅

(III)

CH₃N COC₂H₅

(III)

CH₃N COC₂H₅

CH₃N COC₂H₅

CH₃N COC₂H₅

(III)

CH₃N COC₂H₅

CH₃N COC₂H₅

CH₃N COC₂H₅

CH₃N COC₂H₅

CH₃N COC₂H₅

(III)

CH₃N COC₂H₅

CH₃N COC₂H₅

CH₃N COC₂H₅

(III)

TMSBR: CH₂Cl₂.

Figure 6

Scheme 4. Resolution of 8A, 15A, and 18Aª

$$C_{C_{1}}$$
 $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{2}}$ $C_{H_{3}}$ $C_{C_{1}}$ C_{C

sagents: (i) (ii) (ii) LIOH; (iii) via Schemes 1 & 2.

Figure 7

Scheme 5. Inversion at C6 and C7a

30a: 6-OH (30b: 7-OH)

^a Reagents: (i) C₆H₅COOH, Ph₃P, DEAD; (ii) LiOH, THF.

Figure 8

Scheme 6. Synthesis of Diarylmethoxy Tropanes^a

PReagents: (i) NaBH4; (ii) 4,4'-difluorobenzhydrol, pTSA.